

Professional / Hematology and Oncology / Leukopenias

Lymphocytopenia

Anthony Territo, MD, Emeritus Professor of Medicine, Division of Hematology and Oncology, Geffen School of Medicine at UCLA

Lymphocytopenia is a total lymphocyte count of $< 1000/\mu\text{L}$ in adults or $< 3000/\mu\text{L}$ in children < 2 yr. Sequelae include opportunistic infections and an increased risk of malignant and autoimmune disorders. If the CBC reveals lymphocytopenia, testing for immunodeficiency and analysis of lymphocyte subpopulations should follow. Treatment is directed at the underlying disorder.

Normal lymphocyte count in adults is 1000 to $4800/\mu\text{L}$; in children < 2 yr, 3000 to $9500/\mu\text{L}$. At age 6 yr, the lower limit of normal is $1500/\mu\text{L}$.

Neutrophils and T cells are present in the peripheral blood; about 75% of the lymphocytes are T cells and 25% B cells. Because lymphocytes account for only 20 to 40% of the total WBC count, lymphocytopenia may go unnoticed when WBC count is checked without a differential.

Normal Calculator: Absolute Lymphocyte Count

Approximately 65% of blood T cells are CD4+ (helper) T cells. Most patients with lymphocytopenia have a reduced absolute number of T cells, particularly in the number of CD4+ T cells. The average number of CD4+ T cells in adult blood is $1100/\mu\text{L}$ (range, 300 to $2000/\mu\text{L}$), and the average number of cells of the other major T-cell subgroup, CD8+ (suppressor) T cells, is $600/\mu\text{L}$ (range, 100 to $1500/\mu\text{L}$).

Pathology

Lymphocytopenia can be

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quired

herited

red lymphocytopenia

ed lymphocytopenia can occur with a number of other disorders (see Table: [Causes of Lymphocytopenia](#)). The most on causes include

rotein-energy undernutrition

IDS and certain other viral infections

[n-energy undernutrition](#) is the most common cause worldwide.

the most common infectious disease causing lymphocytopenia, which arises from destruction of CD4+ T cells infected IV. Lymphocytopenia may also reflect impaired lymphocyte production arising from destruction of thymic or lymphoid ctore. In acute viremia due to HIV or other viruses, lymphocytes may undergo accelerated destruction from active ons with the virus, may be trapped in the spleen or lymph nodes, or may migrate to the respiratory tract.

enic lymphocytopenia is caused by cytotoxic chemotherapy, radiation therapy, or the administration of antilymphocyte n (or other lymphocyte antibodies). Long-term treatment for psoriasis using psoralen and ultraviolet A irradiation may y T cells. Glucocorticoids can induce lymphocyte destruction.

ocytopenia may occur with [lymphomas](#), autoimmune diseases such as [SLE](#), [rheumatoid arthritis](#), [myasthenia gravis](#), and n-losing enteropathy.

ited lymphocytopenia

ed lymphocytopenia (see Table: [Causes of Lymphocytopenia](#)) most commonly occurs in

[evere combined immunodeficiency disorder](#)

[Wiskott-Aldrich syndrome](#)

occur with inherited **immunodeficiency disorders** and disorders that involve impaired lymphocyte production. Other ed disorders, such as **Wiskott-Aldrich syndrome**, **adenosine deaminase deficiency**, and **purine nucleoside phosphorylase ncy**, may involve accelerated T-cell destruction. In many disorders, antibody production is also deficient.

Causes of Lymphocytopenia

ism	Examples
d	<p>AIDS</p> <p>Other infectious disorders, including hepatitis, influenza, TB, typhoid fever, and sepsis</p> <p>Dietary deficiency in patients with ethanol abuse, protein-energy undernutrition, or zinc deficiency</p> <p>Protein losing enteropathy</p> <p>Iatrogenic after use of cytotoxic chemotherapy, glucocorticoids, high-dose psoralen and ultraviolet A radiation therapy, lymphocyte antibody therapy, immunosuppressants, radiation therapy, or thoracic duct drainage</p> <p>Systemic disorders with autoimmune features (eg, aplastic anemia, Hodgkin lymphoma, myasthenia gravis, protein-losing enteropathy, RA, chronic kidney disease, sarcoidosis, SLE, thermal injury)</p>
ary	<p>Aplasia of lymphopoietic stem cells</p> <p>Ataxia-telangiectasia</p> <p>Cartilage-hair hypoplasia syndrome</p> <p>Idiopathic CD4+ T lymphocytopenia</p> <p>Immunodeficiency with thymoma</p> <p>Severe combined immunodeficiency associated with a defect in the IL-2 receptor gamma-chain, deficiency of ADA or PNP, or an unknown defect</p> <p>Wiskott-Aldrich syndrome</p>
	<p>adenosine deaminase; PNP = purine nucleoside phosphorylase.</p>

Symptoms and Signs

Lymphocytopenia per se generally causes no symptoms. However, findings of an associated disorder may include

- absent or diminished tonsils or lymph nodes, indicative of cellular immunodeficiency

- skin abnormalities (eg, alopecia, eczema, pyoderma, telangiectasia)

- evidence of hematologic disease (eg, pallor, petechiae, jaundice, mouth ulcers)

- generalized lymphadenopathy and splenomegaly, which may suggest **HIV infection** or **Hodgkin lymphoma**

Lymphocytopenic patients experience recurrent infections or develop infections with unusual organisms. **Pneumocystis jirovecii**, **cytomegalovirus**, **rubeola**, and **varicella** pneumonias often are fatal. Lymphocytopenia is also a risk factor for the development of malignancies and for autoimmune disorders.

Diagnosis

- Clinical suspicion (repeated or unusual infections)

- CBC with differential

- Measurement of lymphocyte subpopulations and immunoglobulin levels

Lymphocytopenia is suspected in patients with recurrent viral, fungal, or parasitic infections but is usually detected incidentally on CBC. *P. jirovecii*, cytomegalovirus, rubeola, or varicella pneumonias with lymphocytopenia suggest immunodeficiency.

Lymphocyte subpopulations are measured in patients with lymphocytopenia. Measurement of immunoglobulin levels should be done to evaluate antibody production. Patients with a history of recurrent infections undergo complete **laboratory evaluation for immunodeficiency**, even if initial screening tests are normal.

Treatment

treatment of associated infections

treatment of underlying disorder

sometimes IV immune globulin

possibly hematopoietic stem cell transplantation

quired lymphocytopenias, lymphocytopenia usually remits with removal of the underlying factor or successful treatment of underlying disorder. IV immune globulin is indicated if patients have chronic IgG deficiency, lymphocytopenia, and recurrent infections. **Hematopoietic stem cell transplantation** can be considered for all patients with congenital immunodeficiencies and is curative.

Key Points

Lymphocytopenia is most often due to AIDS or undernutrition, but it also may be inherited or caused by various infections, drugs, or autoimmune disorders.

Patients have recurrent viral, fungal, or parasitic infections.

Lymphocyte subpopulations and immunoglobulin levels should be measured.

Treatment is usually directed at the cause, but occasionally, IV immune globulin or, in patients with congenital immunodeficiency, stem cell transplantation is helpful.

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